INSTITUTIONAL REVIEW BOARD (IRB) SUBMISSION REQUIREMENTS

A. Protocol Preparation. Protocols will be formulated within the mission areas of Coast Guard (CG) or the Department of Homeland Security (DHS). The problem or objective to be addressed will be stated in clear, concise language. The required elements of a protocol are as follows:

1. Protocol Title. The protocol title must be the same as the project/proposal title unless multiple protocols are being submitted within one proposal.

2. Principal Investigator (PI). Provide the complete name, address, phone number, and email address of the principal investigator. Include a copy of the primary investigator's (PI) curriculum vitae (CV) and certificate of completion of human subject protection training with the protocol. If the protocol involves the use of non-OTC pharmaceuticals, a copy of Good Clinical Practice (GPC) training certificate must also accompany the submitted protocol. To be considered current, training is required within 12 months of submitting any protocol involving drugs/devices. The training may be taken by correspondence or internet-based training, but an on-site course must have occurred no more than 3 years prior to protocol submission. List the names of all personnel who will have significant involvement in the research study; include their practice license (e.g., MD or RN), highest degree(s), job title, and employing institution. In addition, if a Medical Monitor has been assigned to the study, which is required for Greater Than Minimal Risk (GTMR) studies, include his/her name and provide a copy of the current CV.

3. Location of Study. List location(s) where the data is to be collected. If applicable, include the name, degree(s), title, employing institution, and complete address of the investigator(s) for each site.

4. Time Line of Project. State the month and year the project is expected to start, when data collection will be complete, and when final report is expected.

5. Military/Security Relevance. Clearly state the problem to be investigated. Describe how this issue currently impacts the DHS or the CG and what information is to be gained by this research. Include gap analysis, Program Manager or stakeholder endorsement, and/or other research drivers as appropriate. If possible, link products of the proposed research to CG or Homeland Security programs/needs.

6. Introduction/Literature Review. Provide a comprehensive description of previous research relevant to this project. Ensure that an adequate foundation has been laid which shows what knowledge already exists and what information is lacking in this field of study.

7. Objectives. Provide a detailed description of the objectives of the study (what information or technology will be obtained from this project).

8. Study Population. Describe the target population (e.g., all CG personnel, aviators, or those operating on a specific platform or within a specific rate), approximate number, and pertinent demographic characteristics (e.g., age, number of years in service, number of career hours exposed to a particular hazard). Describe the methods that will be used to obtain a sample of subjects from the accessible population (e.g., convenience, simple random, stratified random) together with the inclusion and exclusion criteria (include age, gender, and ethnicity).

    a. If pregnant subjects will be excluded from participation in the study, the method used to determine pregnancy status in women of childbearing potential must be specified. It is the CG's current policy that women volunteers must consent to a serum pregnancy test within 48 hours from the start of all GTMR protocols. Additionally, if the research involves within subjects repeated measures designs (e.g., multiple condition drug tests), subjects will be tested 48 hours prior to administration/conduct of each condition. This procedure may also be required for certain minimal risk protocols if imposed as a condition of subject safety by the medical monitor, or the IRB.

    b. Also, state the time that will elapse between the pregnancy test and exposure to research procedures or medical products and how long the non-pregnant subject should use effective contraceptive practices after participating in the study. Please note that contraceptive practices may be necessary for male subjects participating in certain types of studies.

9. Protocol Design and Methodology. Outline the proposed methodology in sufficient detail to show a clear course of action. Minimum guidance for the plan should include:

    a. Description of the recruitment process, to include copies of all recruitment and advertisement materials for review.

    b. Description of the Informed Consent process. State who will perform the informed consent interview and when the interview will take place relative to the participant beginning study participation. Address how privacy and time for decision-making will be provided and whether or not the potential subject will be allowed to discuss the study with anyone before making a decision. When using a verbal consent procedure, indicate who will serve as the witness to the informed consent interview. Two copies of the consent form should be completed--the subject gets the original copy and a copy is kept for the PI's study records. Electronic copies of these forms can be obtained from the Commandant (CG-113) website http://www.uscg.mil/hq/cg1/cg113/default.asp).

c. Sample size and subject assignment. Describe the process used to calculate sample size to ensure that adequate sample size has been chosen. Describe the method that will be used to assign subjects to various conditions when using between groups designs or the process used to select the order of conditions when using within subject designs (e.g., randomization, matched pairs). Describe the system that will be used to code individual subject data files.

d. Study evaluations. List and describe any evaluations (e.g., laboratory procedures, history, or physical examination) that are required to determine eligibility for study participation. Describe any evaluations to be made during the conduct of the study (e.g., laboratory, psychological, etc.). Also, describe data handling requirements (e.g., specimens to be collected; schedule and amounts; storage, to include where and whether special conditions are required; labeling; and disposition).

e. Assessments. Provide a copy of data collection forms, questionnaires, rating scales, and/or interview guides that will be used in the study (e.g., cognitive, reaction time, simulated or actual task performance, and mood assessments). Include a copy of the scenario if the protocol involves data collection under simulated conditions.

f. Describe the research intervention or activity that the subject will experience. Provide sufficient detail in chronological order for a person uninvolved in the research to understand what the subject will experience. If the protocol involves repeated measures, include a test schedule that clearly conveys the time required by each volunteer to complete the study.

g. Describe the statistical analysis plan. Include any analyses which might be conducted prior to collection of full data set (for example, to ensure sample size will be adequate to draw conclusions). Describe the statistical design and corresponding rationale in detail.

h. References. Provide a current and fully annotated bibliography/reference section based upon a detailed literature review in the introduction.

i. Budget. Include an estimate of man hours, salary requirements, equipment, travel costs and other expenses which might be incurred during the conduct of the research.

10. <u>Risks/Benefits Assessment</u>.

a. Describe risks (e.g., physical, psychological, social, economic, legal, and privacy/confidentiality risks) associated with the research, measures to be taken to minimize and/or eliminate risks or to manage unpreventable risks and

special medical or nursing care that will be needed prior to, during, or following participation.

b. Describe benefits of the research to the subject. If there will be no benefits to the subjects (other than knowing he/she has contributed to science), state this in the protocol and consent form.

c. Payment or compensation for participation is not considered to be a benefit and must be addressed in a separate section.

11. Reporting of Serious or Unexpected Adverse Events.

a. Adverse Events (AEs) and Serious or Unexpected Adverse Events (SAEs) can occur in the conduct of any research project. Include a definition of what constitutes an AE or SAE in the study. Electronic copies of the sample definitions and reporting forms can be found on the Commandant (CG-113) website http://www.uscg.mil/hq/cg1/cg113/default.asp).

b. All research protocols must address the following requirements:

An AE temporally related to participation in the study should be documented whether or not considered related to the test article or procedure. This definition includes current illnesses and injuries and exacerbations of preexisting conditions including changes to psychological state. Include the following in all Investigation New Drug (IND) and Investigational Device (ID) safety reports: subject identification number and initials; principal investigator's name and name of CG clinic or DoD Military Treatment Facility (MTF); subject's age, gender, and ethnicity; test article/procedure and dates of administration; signs/symptoms and severity; date of onset; date of resolution or death; relationship to the study drug, event or procedure; action taken; concomitant medication(s) including dose, route and duration of treatment; and date of last dose, if applicable.

c. Describe agencies or offices to be notified with point of contact information in the event of a serious and unexpected adverse event. For all protocols involving human subjects, including investigational new drug or device studies, the following information about reporting serious and SAE, must be included in the protocol:

(1) Unanticipated problems involving risk to subjects or others, serious or life-threatening adverse events related to participation in a research study, and all subject deaths, should be promptly reported by telephone (202-475-5166) or by facsimile (202-475-5926) to the CG IRB Chair.

(2) A complete written report will follow the initial notification. The written report will be sent thru the IRB Chair to the Commandant (CG-

11) for review. In addition to the methods above, the complete report shall be sent to: COMMANDANT (CG-11), US COAST GUARD, 2100 2ND ST SW STOP 7902, WASHINGTON DC 20593-7902.

d. Adverse events that are not deemed to be serious by the medical monitor will be recorded and placed in the individual subject study files and reported to the CG IRB Chair within 10 days. These events may be recorded on an AE form (see Enclosure (3) for a sample form) or on an IRB pre-approved check sheet which covers these types of events (e.g., slight headache, complaints of tired eyes, slight upset stomach following simulator flight). Electronic copies of the sample reporting forms can be found on the Commandant (CG-113) website. This information will be tallied at the conclusion of testing and submitted as part of the final report necessary for protocol completion and closure.

12. Description of Protocol Drugs or Devices. If the protocol uses an investigational drug or device, provide the following information:

a. IND/IDE number and name of sponsor.

b. Complete names and composition of all medication(s), device(s), or placebo(s).

c. Source of medications, devices, or placebos.

d. Location of storage for study medications.

e. Dose range, schedule, and administration of test articles.

f. Washout period, if used, should be described in detail.

g. Duration of drug or device treatment.

h. Concomitant medications allowed.

i. Antidotes and treatments available.

j. Disposition of unused drug.

k. The procedure by which the IND sponsor will monitor the protocol in accordance with reference (e).

l. In addition to the above list of requirements to address in the protocol, include the following with the protocol submission:

(1) A copy of the Investigator's Brochure and/or device manual and associated case report/data collection forms.

(2) A signed Form FDA 1572 for IND Applications that have been approved by the FDA, including the following information (for non-FDA new drug protocols, the following information should be included in the protocol):

1. Name, address, and a statement of the qualifications for each investigator and the name of each sub-investigator working under the PI.

2. Names and addresses of facilities to be used.

3. Name and address of each IRB reviewing the protocol.

(3) For Investigational Devices, include CG's IRB assessment of the risk, such as minimal or GTMR of the investigational device you plan to use in your study. If the device poses significant risk to research subjects, specify the IDE number obtained from the FDA, the name of the sponsor, and the procedure by which the IDE sponsor will monitor the protocol in accordance with Code of Federal Regulations.

13. Disposition of Data. Describe where data will be stored, who will keep the data, how the data will be stored, and the length of time data will be stored. Note that records of IND studies must be kept until 2 years after a New Drug Application is approved/issued, or for 2 years after the IND is withdrawn (ICH Harmonized Tripartite Guideline for Good Clinical Practice). Records required for IDE studies should be retained for 2 years after the latter of the following dates: the date that the investigation is terminated or completed and the date that the records are no longer required for support of the pre-market approval application.

14. Amendment of the Protocol. Describe the procedures to be followed if the protocol is to be modified, amended or terminated before completion. Note that any modification to the protocol, consent form and/or questionnaires must be submitted to the CG IRB for review and approval.

15. Departure from the Protocol. Describe procedures and notifications to be made in the event of deviations from the approved protocol requirements.

16. Roles and Responsibilities of Study Personnel. Briefly describe the duties of all study personnel, which should include each of the persons listed as investigators, research staff, consultants, and the medical monitor. Describe their roles in the research effort (e.g., Research Coordinator, 80%, recruit and consent subjects, maintain study records, administer study drug, take and record vital signs, enter data into computer data base). At least one CG PI is normally required on every CG protocol (to include test and evaluation).

17. Investigators conducting GTMR research must include the following description of requirements of the Volunteer Registry Database (VRDB) in the protocol and consent

form:

a. It is the policy of the CG that data sheets are to be completed on all volunteers participating in research for entry into the USCG VRDB. The information to be entered into this confidential database includes name, address, employee identification number, study name, and dates. The intent of the database is two-fold: first, to readily answer questions concerning an individual's participation in research sponsored by CG, and second, to ensure that the CG can exercise its obligation to ensure research volunteers are adequately warned (duty to warn) of risks and to provide new information as it becomes available. The CG IRB will maintain VRDB records for a minimum of 5 years.

b. Include in the protocol language to indicate that the VRDB sheets must be completed. In addition, include the completion of the VRDB sheets in the study procedure timelines. A copy of the VRDB form can be found on the Commandant (CG-113) website (http://www.uscg.mil/hq/cg1/cg113/default.asp). The data sheets must be sent to the following address: COMMANDANT (CG-11), U.S. COAST GUARD, 2100 2ND ST SW STOP 7902, WASHINGTON DC 20593-7902.

c. VRDB sheets shall be submitted annually and upon completion of the study. Use of the VRDB sheets is not required for Exempt or Minimal Risk studies, unless otherwise indicated.

18. If subjects will be recruited through an advertisement, newspaper article, or similar process, a copy of the approved advertisement must be provided.

19. For studies involving investigational drugs or devices the FDA has established guidelines on advertisements for subjects. General guidance includes name and address of PI, summary of research purpose, brief eligibility criteria, truthful list of benefits, and the person to contact for further information.

20. If the research involves surveys, questionnaires, or other instruments, include a copy of the most recent IRB-approved version of each of these documents with the protocol submission. For either of these instruments that are used, the following information at a minimum should be addressed:

    a. The instrument should be labeled with the complete title of the study and instructions for completing and returning the instrument.

    b. The instructions should state that the subject can refuse to answer specific items without repercussions.

    c. Address whether the instrument has been validated.

    d. The instructions should be comprehensible and unambiguous.

21. Describe the procedure for confidentiality of hardcopy or electronic data in the protocol and consent form.